

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

### **IN THE CLAIMS**

This listing of claims replaces all prior versions and listings of the claims in this application:

Claims 1-13 (Canceled)

13. (Currently amended) A system for performing PCR and monitoring the reaction during temperature cycling comprising;

a chamber;

a plurality of sample containers each for holding a PCR sample, each sample container comprising walls composed of an optically transparent material and defining a volume having a first and second dimension, wherein the first dimension is less than the second dimension and the ratio of volume to external surface area of the container is less than 1 mm, each sample container formed for holding ~~less a maximum volume of than~~ 1 milliliter of a sample;

a rotatable carousel rotatably mounted within said chamber and formed for holding said plurality of samples, wherein said carousel moves the sample containers one by one to a monitoring position located within said chamber;

a forced air heater for simultaneously heating all the PCR samples in the carousel;

means for simultaneously cooling all the PCR samples in the carousel;

control means for repeatedly operating the forced air heater and the means for cooling to subject the PCR sample to thermal cycling within said chamber;

means for optically exciting the sample in the monitoring position to cause the sample to fluoresce; and

means for detecting the fluorescence of the excited sample during amplification when the sample is in the monitoring position.

14. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 13 further comprising:

means for determining at least one reaction parameter in accordance with the detected fluorescence.

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

15. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 14 further comprising means for adjusting the control means in accordance with the reaction parameter.

16. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 15 in which the control means adjusts the operation of the forced air heater and the means for cooling to alter the times the means for heating and the means for cooling operate in accordance with the reaction parameter.

17. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 15 in which the control means adjusts the operation of the forced air heater and the means for cooling to alter the rate at which the biological sample is heated and cooled in accordance with the reaction parameter.

18. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 13 wherein the sample containers are fabricated at least partially from glass, wherein the sample container comprises a capillary tube, that is closed at one end, with an inner capillary tube wall diameter of about 0.25 mm to about 1.0mm and having a volume not greater than about 100  $\mu$ l.

19. (Cancelled)

20. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 13 further comprising means for positioning the means for optically exciting the sample and the means for detecting the fluorescence of excited sample to optimize the fluorescence which is detected.

21. (Canceled)

22. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 13 wherein the means for cooling

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

comprises an air movement mechanism which transports ambient air to the sample containers.

23. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 13 wherein the control means comprises a microprocessor.

24. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 13 wherein the means for optically exciting the sample comprises a photo emitter structure positioned so that the radiation emitted therefrom impinges the first side of the sample container in the monitoring position.

25. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 24 wherein means for detecting the fluorescence of the excited sample comprises a photo detector structure positioned so that the radiation emitted from the second side of the sample container in the monitoring position is detected.

26. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 13 wherein the means for optically exciting the sample comprises a photo emitter structure positioned so that the radiation emitted therefrom impinges the end of the sample container in the monitoring position.

27. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 26 wherein the means for detecting the fluorescence of the excited sample comprises a photo detector structure positioned so that the radiation emitted from the end of the sample container in the monitoring position is detected.

28. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 14 wherein the means for determining at least one reaction parameter in accordance with the detected fluorescence

Appl. No. 08/869,275  
Reply to Office Action of November 14, 2005

comprises means for determining at least one reaction parameter selected from the group consisting of: product melting temperature, product melting time, product reannealing temperature, product reannealing time, probe melting time, primer annealing/extension temperature, and primer annealing/extension time.

29. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 13 wherein the control means comprises means for cooling the sample when the means for detecting the fluorescence of the excited sample detects that the product is completely melted.

30. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 13 wherein the control means comprises means for heating the sample when the means for detecting the fluorescence of the excited sample detects no more product generation.

31. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 13 wherein the means for optically exciting is positioned to interact with the first side of the sample container in the monitoring position and the means for detecting the fluorescence is positioned to interact with the second side of the sample container in the monitoring position.

32. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 13 wherein the means for optically exciting is positioned to interact with the end of the sample container and the means for detecting the fluorescence is positioned to interact with the end of the sample container.

33. (Currently amended) A system for performing PCR and monitoring the reaction in real time during temperature cycling comprising:

a chamber;

a plurality of sample containers for holding a plurality of PCR samples, each sample container comprising an optically clear capillary tube, each sample container formed for

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

holding a maximum volume of less than 1 milliliter of a sample and having a sealed end and an open end with a sealable closure on the open end;

a rotatable carousel, rotatably mounted within said chamber and formed for holding the sample containers, to move the sample containers one by one to a monitoring position, said monitoring position located within said chamber;

means for forcing hot gas into contact with the plurality of sample containers in the carousel;

means for forcing cool gas into contact with the plurality of sample containers in the carousel;

means for repeatedly operating the means for forcing hot gas and the means for forcing cool gas to subject the PCR samples to thermal cycling within said chamber;

means for optically exciting at least one selected PCR sample to cause the selected PCR sample to fluoresce;

means for detecting the fluorescence of the excited selected PCR sample at both a first wavelength and a second wavelength; and

means for determining at least one reaction parameter for the selected PCR sample in accordance with the fluorescence at the first and second wavelengths and displaying the reaction parameter in a visually perceptible manner in real time.

34. (Previously presented) A system for performing PCR and monitoring the reaction in real time during temperature cycling as defined in claim 33 further comprising means for adjusting the means for repeatedly operating in accordance with the reaction parameter such that the reaction is adjusted in real time.

35. (Previously presented) A system for performing PCR and monitoring the reaction in real time during temperature cycling as defined in claim 33 wherein the means for determining at least one reaction parameter in accordance with the detected fluorescence at the first and second wavelengths and displaying the reaction parameter in a visually perceptible manner in real time comprises means for determining a reaction parameter selected from the group consisting of denaturation temperature and time, primer annealing temperature and time, probe annealing temperature and time, enzyme extension temperature and time, and number of cycles.

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

Claims 36-54 (Canceled)

55. (Currently amended) A system for carrying out and monitoring the progress of first and second biological reactions comprising:

a chamber;

first holding means for holding a first biological sample;

second holding means for holding a second biological sample;

transporting means for moving the first and second holding means between a non monitoring position and a monitoring position, wherein said transporting means and said monitoring and non monitoring positions are located with in said chamber;

thermal cycling means for repeatedly heating and cooling the first holding means and the second holding means in both the non monitoring position and in the monitoring position to carry out thermal cycling simultaneously on both the first biological sample and the second biological sample to generate a first and second biological reaction, the thermal cycling means comprising a forced air heater and a fan;

monitoring means for ascertaining the progress of the first biological reaction in the first means for holding and the second biological reaction in the second means for holding, the means for monitoring comprising means for detecting radiation emitted from the first and second biological reactions, when the first and second biological reaction are sequentially positioned in the monitoring position; and

controlling means for controlling the operation of the transporting means, thermal cycling means, and the monitoring means such that the progress of the first and second biological reactions is detected as thermal cycling occurs.

56. (Previously presented) A system for carrying out and monitoring the progress of first and second biological reactions as defined in claim 55 wherein the monitoring means comprises:

an excitation source emitting excitation radiation;

means for directing the excitation radiation to the monitoring position such that when the first or second biological samples are located at the monitoring position the samples emit radiation;

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

means for converting the emitted radiation to an electrical signal;  
means for processing the electrical signal to arrive at a reaction parameter;  
means for displaying the reaction parameter; and  
means for recording the reaction parameter.

57. (Previously presented) A system for carrying out and monitoring the progress of first and second biological reactions as defined in claim 56 wherein the reaction parameter is selected from the group consisting of denaturation temperature and time, primer annealing temperature and time, probe annealing temperature and time, enzyme extension temperature and time, and number of cycles.

58. (Previously presented) A system for carrying out and monitoring the progress of first and second biological reactions as defined in claim 56 wherein:

the excitation source comprises a photo-emitting source, the photo-emitting source selected from the group consisting of a xenon lamp and a light emitting diode;

the means for converting the emitted radiation to an electrical signal comprises a photo-detection device, the photo-detection device selected from the group consisting of a photo-multiplier tube and a photo-diode; and

the means for processing the electrical signal to arrive at a reaction parameter comprises a microprocessor.

59. (Previously presented) A system for carrying out and monitoring the progress of first and second biological reactions as defined in claim 58 wherein the means for converting the emitted radiation to an electrical signal comprises a first photo-detection device, the first photo-detection device is selected from the group consisting of a photo-multiplier tube and a photo-diode and a second photo-detection device selected from the group consisting of a photo-multiplier tube and a photo-diode.

Claims 60-78 (Cancelled)

79. (Previously presented) A device for monitoring the fluorescence of a plurality of samples each held within its respective sample vessel, said device comprising

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

a chamber;

a carousel for holding a plurality of sample vessels and moving each sample vessel sequentially to a monitoring position, said carousel being rotatably mounted in said chamber, and each sample vessel comprising an optically transparent material and walls defining a volume having at least first and second dimensions wherein the first dimension is less than the second dimension and wherein the ratio of volume to external surface area of the vessel is less than 1mm;

a stepper motor for rotating said carousel;

means for coupling said carousel to said motor;

a forced air heater and a fan in air flow communication with the chamber and a controller therefor for rapidly cycling the temperature of the chamber;

a light emitting source mounted in said chamber and positioned to illuminate the sample vessel in the monitoring position along an axis substantially parallel to a wall along the second dimension of the vessel; and

a light detector mounted in said chamber and positioned to measure fluorescence from the sample vessel in the monitoring position along an axis substantially parallel to a wall along the second dimension of the vessel.

80. (Previously presented) The device of claim 79 wherein said sample vessels are capillary tubes.

81. (Cancelled)

82. (Currently amended) A device for conducting PCR reactions, said device comprising a chamber;

a forced air heater and a fan mounted in said device and in air flow communication with the chamber;

a carousel for holding a plurality of sample vessels, said carousel being rotatably mounted in said chamber to move the sample vessels one by one to a monitoring position, said heater and fan positioned to supply hot or cool air simultaneously to each of the plurality of sample vessels held in the carousel;



Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

each of said sample vessels comprising an optically transparent material and walls defining a volume having at least first and second dimensions wherein the first dimension is less than the second dimension and wherein the ratio of volume to external surface area of each of said sample vessels is less than 1mm, each sample container formed for holding a maximum volume of 1 milliliter of a sample;

a light emitting source mounted in said chamber and positioned to illuminate at least one selected sample vessel in the monitoring position along an axis substantially parallel to a wall along the second dimension of the selected sample vessel; and

a light detector mounted in said chamber and positioned to measure fluorescence from the selected sample vessel in the monitoring position along an axis substantially parallel to a wall along the second dimension of the selected sample vessel.

Claims 83-120 (Cancelled)

121. (Currently amended) A device for conducting PCR reactions, said device comprising

a chamber;

a forced air heater and a fan mounted in said device and in air flow communication with the chamber;

a carousel for holding a plurality of sample vessels, said carousel being rotatably mounted in said chamber to move the sample vessels sequentially to a monitoring position, the carousel positioned such that each of the samples in the carousel are simultaneously heated or cooled by air flow directed by said mounted fan;

said sample vessels comprising an optically transparent material and walls, wherein said walls define a volume having at least first and second dimensions wherein the first dimension is less than the second dimension and wherein the ratio of volume to external surface area of each of said sample vessels is less than 1mm, each sample container formed for holding a maximum volume of 1 milliliter of a sample;

a light emitting source positioned to illuminate the selected sample vessel in the monitoring position along an axis substantially parallel to a wall along the second dimension of the selected sample vessel;

Appl. No. 08/869,275  
Reply to Office Action of November 14, 2005

a light detector positioned to measure fluorescence from the selected sample vessel in the monitoring position along an axis substantially parallel to a wall along the second dimension of the selected sample vessel.

122. (Previously presented) A system for performing PCR and monitoring the reaction comprising:

a chamber;

a heater and a fan in air flow communication with the chamber and a controller for cycling the temperature in the chamber according to initial predefined temperature and time parameters;

a carousel for holding a plurality of sample vessels said carousel being rotatably mounted in said chamber to move the sample vessels sequentially to a monitoring position, the carousel positioned such that the heater and the fan simultaneously heat and cool each of the samples in the carousel, said sample vessels comprising an optically transparent material and walls defining a volume having at least first and second dimensions wherein the first dimension is less than the second dimension and wherein the ratio of volume to external surface area of the vessel is less than 1mm;

a light emitting source positioned to illuminate the sample vessel in the monitoring position along an axis substantially parallel to a wall along the second dimension of the vessel;

a light detector positioned to measure fluorescence from the sample vessel in the monitoring position along an axis substantially parallel to a wall along the second dimension of the vessel; and

means for displaying the status of the reaction based detected fluorescence.

123. (Previously presented) The system of claim 122 further comprising means for adjusting the controller such that one or more reaction parameters the reaction is adjusted during temperature cycling.

124. (Previously presented) The system of claim 122 wherein the carousel comprises:

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

a disc having a top surface, a bottom surface, an outer edge extending therebetween, a sample receiving port in the top surface, a sample vessel port in the outer edge, and a sample passageway communicating with said sample receiving port and the sample vessel port, said sample vessel port and passageway formed for receiving and fixing a sample vessel to the disc.

125. (Previously presented) The system of claim 122 wherein the sample vessels are capillary tubes each having an inner diameter ranging from about 0.02 mm to about 1.0 mm.

126. (Previously presented) The system of claim 124 wherein the passageway of the carousel includes a barrier that prevents a liquid sample delivered through the sample receiving port from flowing to the sample vessel port absent a biasing force on said liquid sample.

127. (Previously presented) The system of claim 124 further comprising a motor for rotating the carousel to provide a biasing force on a liquid sample delivered through the sample receiving port.

128. (Currently amended) A system for performing PCR and monitoring the reaction during temperature cycling comprising;

a chamber

a plurality of sample containers, each sample container comprising walls composed of an optically transparent material and defining a volume having a first and second dimension, wherein the first dimension is less than the second dimension and the ratio of volume to external surface area of the container is less than 1 mm, wherein each sample container is formed for holding a maximum volume of less than 1 milliliter of a sample;

means for moving the sample containers sequentially into and out of a monitoring position located with in the chamber;

a forced air heater for heating each PCR sample simultaneously within said chamber, regardless of whether ~~it~~ the sample is in or out of the monitoring position, at a rate of at least 0.5°C/second;

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

means for cooling each PCR sample simultaneously within said chamber, regardless of whether it is in or out of the monitoring position, at a rate of at least 0.5°C/second;

control means for repeatedly operating the forced air heater, when the means for detecting the fluorescence of the excited sample detects no more product generation, and the means for cooling, when the means for detecting the fluorescence of the excited sample detects that the product is completely melted, to subject the PCR sample to thermal cycling;

means for optically exciting the sample in the monitoring position within said chamber to cause the sample to fluoresce;

means for detecting the fluorescence of the excited sample during amplification when the sample container is in the monitoring position;

means for determining at least one reaction parameter in accordance with the detected fluorescence; and

means for adjusting the control means in accordance with the reaction parameter.

129. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 128 in which the control means adjusts the operation of the means for heating and the means for cooling to alter the times the forced air heater and the means for cooling operate in accordance with the reaction parameter.

130. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 128 in which the control means adjusts the operation of the forced air heater and the means for cooling to alter the rate at which the biological sample is heated and cooled in accordance with the reaction parameter.

131. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 128 wherein the means for moving the PCR sample containers comprises a rotatable carousel.

132. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 128 further comprising means for

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

positioning the means for optically exciting the sample and the means for detecting the fluorescence of excited sample to optimize the fluorescence which is detected.

133. (Cancelled)

134. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 128 wherein the means for cooling comprises an air movement mechanism which transports ambient air to the sample container.

135. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 128 wherein the control means comprises a microprocessor.

136. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 128 wherein the means for optically exciting the sample comprises a photo emitter structure positioned so that the radiation emitted therefrom impinges the first side of the sample container in the monitoring position.

137. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 136 wherein means for detecting the fluorescence of the excited sample comprises a photo detector structure positioned so that the radiation emitted from the second side of the sample container in the monitoring position is detected.

138. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 128 wherein the means for optically exciting the sample comprises a photo emitter structure positioned so that the radiation emitted therefrom impinges the end of the sample container in the monitoring position.

139. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 138 wherein the means for detecting the fluorescence of the excited sample comprises a photo detector structure positioned so that

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

the radiation emitted from the end of the sample container in the monitoring position is detected.

140. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 128 wherein the means for determining at least one reaction parameter in accordance with the detected fluorescence comprises means for determining at least one reaction parameter selected from the group consisting of: product melting temperature, product melting time, product reannealing temperature, product reannealing time, probe melting time, primer annealing/extension temperature, and primer annealing/extension time.

Claims 141-144 (Canceled)

145. (Currently amended) A system for performing PCR and monitoring the reaction in real time during temperature cycling comprising:

a chamber

a plurality of sample containers for holding a plurality of PCR samples, each sample container comprising an optically clear capillary tube, each sample container formed for holding a maximum volume of less than 1 milliliter of a sample and having a sealed end and an open end with a sealable closure on the open end;

a rotatable carousel rotatably mounted within said chamber and formed for holding the sample containers to move the sample containers one by one to a monitoring position, said monitoring position located within said chamber;

means for forcing hot gas into contact with the plurality of sample containers in the carousel;

means for forcing cool gas into contact with the plurality of sample containers in the carousel;

means for repeatedly operating the means for forcing hot gas and the means for forcing gas fluid to subject the PCR samples to thermal cycling within said chamber;

means for optically exciting at least one selected PCR sample in the monitoring position to cause the selected PCR sample to fluoresce;

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

means for detecting the fluorescence of the excited selected PCR sample in the monitoring position at both a first wavelength and a second wavelength;

means for determining at least one reaction parameter for the selected PCR sample in accordance with the detected fluorescence at the first and second wavelengths and displaying the reaction parameter in a visually perceptible manner in real time; and

means for adjusting the means for repeatedly operating in accordance with the reaction parameter such that the reaction is adjusted in real time.

146. (Previously presented) A system for performing PCR and monitoring the reaction in real time during temperature cycling as defined in claim 145 wherein the means for determining at least one reaction parameter in accordance with the detected fluorescence at the first and second wavelengths and displaying the reaction parameter in a visually perceptible manner in real time comprises means for determining a reaction parameter selected from the group consisting of denaturation temperature and time, primer annealing temperature and time, probe annealing temperature and time, enzyme extension temperature and time, and number of cycles.

147. (Previously presented) A system for performing PCR and monitoring the reaction in real time comprising;

a chamber;

a heater and a fan mounted in air flow communication with the chamber and a controller for cycling the temperature in the chamber according to initial predefined temperature and time parameters;

a carousel for holding a plurality of sample vessels said carousel being rotatably mounted in said chamber to move the sample vessels sequentially to a monitoring position, said sample vessels comprising an optically transparent material and walls defining a volume having at least first and second dimensions wherein the first dimension is less than the second dimension and wherein the ratio of volume to external surface area of the vessel is less than 1mm;

a light emitting source mounted in said chamber and positioned to illuminate at least one of the sample vessels in the monitoring position along an axis substantially parallel to a wall along the second dimension of the vessel;

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

a light detector mounted in said chamber and positioned to measure fluorescence from at least one of the sample vessels in the monitoring position along an axis substantially parallel to a wall along the second dimension of the vessel;

means for displaying the status of the reaction based detected fluorescence; and

means for adjusting the controller such that one or more reaction parameters the reaction is adjusted in real time.

148. (Previously presented) The system of claim 147 wherein the carousel comprises:

a disc having a top surface, a bottom surface, an outer edge extending therebetween, a sample receiving port in the top surface, a sample vessel port in the outer edge, and a sample passageway communicating with said sample receiving port and the sample vessel port, said sample vessel port and passageway formed for receiving and fixing a sample vessel to the disc.

149. (Previously presented) The system of claim 148 wherein the passageway of the carousel includes a barrier that prevents a liquid sample delivered through the sample receiving port from flowing to the sample vessel port absent a biasing force on said liquid sample.

150. (Previously presented) The system of claim 149 further comprising a motor for rotating the carousel to provide the biasing force on the liquid sample to deliver the liquid sample through the sample receiving port.

151. (Previously presented) The system of claim 147 wherein the sample vessels are capillary tubes having an inner diameter ranging from about 0.02mm to about 1.0mm.

152. (Currently amended) A system for performing PCR and monitoring the reaction comprising:

a chamber;



Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

a heater and a fan in air flow communication with the chamber and a controller for cycling the temperature in the chamber according to initial predefined temperature and time parameters;

a carousel for holding a plurality of sample vessels said carousel being rotatably mounted in said chamber to move the sample vessels one by one to a monitoring position located within said chamber; the carousel comprising a disc having a top surface, a bottom surface, and an outer edge extending therebetween, a sample receiving port in the top surface, a sample vessel port in the outer edge, and a sample passageway communicating with said sample receiving port and the sample vessel port, said sample vessel port and passageway formed for receiving and fixing a sample vessel to the disc; the passageway including a barrier that prevents a liquid sample delivered through the sample receiving port from flowing to the sample vessel port absent a biasing force on said liquid sample;

a motor for rotating the carousel to provide a biasing force on a liquid sample delivered through the sample receiving port;

said sample vessels comprising an optically transparent material and walls defining a volume having at least first and second dimensions wherein the first dimension is less than the second dimension and wherein the ratio of volume to external surface area of the vessel is less than 1mm;

a light emitting source positioned to illuminate at least one of the sample vessels in the monitoring position along an axis substantially parallel to a wall along the second dimension of the vessel;

a light detector positioned to measure fluorescence from at least one of the sample vessels in the monitoring position along an axis substantially parallel to a wall along the second dimension of the vessel; and

a display for displaying the status of the reaction based detected fluorescence.

153. (Cancelled).

154. (Previously presented) The system of claim 152 further comprising an adjuster for adjusting the controller such that one or more reaction parameters the reaction is adjusted in real time.

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

155. (Previously presented) The system of claim 152 wherein the sample vessels are capillary tubes each having an inner diameter ranging from about 0.02 mm to about 1.0 mm.

156. (Previously presented) The system of claim 13 further comprising a movable platform on which the means for optically exciting and means for detecting are mounted.

157. (Previously presented) The system of claim 13 wherein the means for detecting the fluorescence of the excited sample during amplification detects fluorescence throughout temperature cycling.

158. (Previously presented) The system of claim 13 wherein the means for detecting the fluorescence of the excited sample during amplification detects fluorescence during an extension or combined annealing/extension phase of temperature cycling.

159. (Cancelled)

160. (Previously presented) The system of claim 13 wherein the rate of heating the PCR sample and the rate of cooling the PCR sample is at least 4.0°C/second.

Claims 161-168 (Cancelled)

169. (Previously presented) The system for carrying out and monitoring the progress of first and second biological reactions as defined in claim 55 wherein the thermal cycling means heats and cools the first biological sample and the second biological sample at a rate of at least 1.0°C/second.

170. (Previously presented) The system for carrying out and monitoring the progress of first and second biological reactions as defined in claim 55 wherein the thermal cycling means heats and cools the first biological sample and the second biological sample at a rate of at least 4.0°C/second.

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

171. (Previously presented) The system for carrying out and monitoring the progress of first and second biological reactions as defined in claim 55 wherein the thermal cycling means heats and cools the first biological sample and the second biological sample at a rate of at least 10°C/second.

172. (Previously presented) The system for carrying out and monitoring the progress of first and second biological reactions as defined in claim 55 wherein the thermal cycling means heats and cools the first holding means and the second holding means at a rate of at least 200°C/second.

173. (Currently amended) A system for performing PCR and monitoring the reaction during temperature cycling comprising;

a chamber;

a sample container for holding a PCR sample, the sample container comprising walls composed of an optically transparent material and defining a volume having a first and second dimension, wherein the first dimension is less than the second dimension and the ratio of volume to external surface area of the container is less than 1 mm, each sample container formed for holding a maximum volume of less than 1 milliliter of a sample ;

means for positioning the PCR sample container in a monitoring position, said monitoring position located within said chamber;

means for heating the PCR sample at a rate of at least 10°C/second;

means for cooling the PCR sample at a rate of at least 10°C/second;

control means for repeatedly operating the means for heating and the means for cooling to subject the PCR sample to thermal cycling within said chamber;

means for optically exciting the sample in the monitoring position to cause the sample to fluoresce; and

means for detecting the fluorescence of the excited sample during amplification when the sample is in the monitoring position.

174. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 173 further comprising:

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

means for determining at least one reaction parameter in accordance with the detected fluorescence.

175. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 174 further comprising means for adjusting the control means in accordance with the reaction parameter.

176. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 175 in which the control means adjusts the operation of the means for heating and the means for cooling to alter the times the means for heating and the means for cooling operate in accordance with the reaction parameter.

177. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 175 in which the control means adjusts the operation of the means for heating and the means for cooling to alter the rate at which the biological sample is heated and cooled in accordance with the reaction parameter.

178. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 173 wherein the sample container is fabricated at least partially from glass, the sample container having a volume of about 100  $\mu$ l.

179. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 173 wherein the means for positioning the PCR sample container in a monitoring position comprises a rotatable carousel.

180. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 173 further comprising means for positioning the means for optically exciting the sample and the means for detecting the fluorescence of excited sample to optimize the fluorescence which is detected.

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

181. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 173 wherein the means for heating the PCR sample comprises a forced air heater.

182. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 173 wherein the means for cooling comprises an air movement mechanism which transports ambient air to the sample container.

183. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 173 wherein the control means comprises a microprocessor.

184. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 173 wherein the means for optically exciting the sample comprises a photo emitter structure positioned so that the radiation emitted therefrom impinges the first side of the sample container.

185. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 184 wherein means for detecting the fluorescence of the excited sample comprises a photo detector structure positioned so that the radiation emitted from the second side of the sample container is detected.

186. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 173 wherein the means for optically exciting the sample comprises a photo emitter structure positioned so that the radiation emitted therefrom impinges the end of the sample container.

187. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 186 wherein the means for detecting the fluorescence of the excited sample comprises a photo detector structure positioned so that the radiation emitted from the end of the sample container is detected.

Appl. No. 08/869,275

Reply to Office Action of November 14, 2005

188. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 174 wherein the means for determining at least one reaction parameter in accordance with the detected fluorescence comprises means for determining at least one reaction parameter selected from the group consisting of: product melting temperature, product melting time, product reannealing temperature, product reannealing time, probe melting time, primer annealing/extension temperature, and primer annealing/extension time.

189. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 173 wherein the control means comprises means cooling the sample when the means for detecting the fluorescence of the excited sample detects that the product is completely melted.

190. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 173 wherein the control means comprises means for heating the sample when the means for detecting the fluorescence of the excited sample detects no more product generation.

191. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 173 wherein the means for optically exciting is positioned to interact with the first side of the sample container and the means for detecting the fluorescence is positioned to interact with the second side of the sample container.

192. (Previously presented) A system for performing PCR and monitoring the reaction during temperature cycling as defined in claim 173 wherein the means for optically exciting is positioned to interact with the end of the sample container and the means for detecting the fluorescence is positioned to interact with the end of the sample container.

193. (Previously presented) The system of claim 173 wherein the rate of heating the PCR sample and the rate of cooling the PCR sample is at least 20°C/second.

Appl. No. 08/869,275  
Reply to Office Action of November 14, 2005

194. (Currently amended) A system for carrying out and monitoring the progress of first and second biological reactions comprising:

a chamber;

first holding means for holding a first biological sample;

second holding means for holding a second biological sample;

transporting means for moving the first and second holding means between a non monitoring position and a monitoring position, wherein said transporting means and said monitoring and non monitoring positions are all located with in said chamber;

thermal cycling means for repeatedly heating and cooling the first biological sample and the second biological sample, in both the non monitoring position and in the monitoring position, at a rate of at least 10°C/second;

monitoring means for ascertaining the progress of the first biological reaction in the first means for holding and the second biological reaction in the second means for holding when the first and second biological samples are in the monitoring position, the means for monitoring comprising means for detecting radiation emitted from the first and second biological samples; and

controlling means for controlling the operation of the transporting means, thermal cycling means, and the monitoring means such that the progress of the first and second biological reactions is detected as thermal cycling occurs.

195. (Previously presented) The system of claim 194 wherein the thermal cycling means heats and cools the first biological sample and the second biological sample at a rate of at least 20°C/second.

196. (Cancelled)

197. (Previously presented) The system of claim 13 wherein the rate of heating the PCR sample and the rate of cooling the PCR sample is at least 1.0°C/second.